Appendix for "Opioid agonist treatment and risk of mortality during an opioid overdose public health emergency: A population-based retrospective cohort study"

Section A1. Cohort construction

We identified individuals with at least one OAT medication dispensation or prescription in PharmaNet (**Table A1**) given that Drug Identification Numbers (DINs) or Product Identification Numbers (PINs) for OAT are specifically allocated for opioid use disorder treatment (as opposed to the treatment of pain, for which methadone (methadone) and buprenorphine/naloxone (buprenorphine/naloxone) are rarely used and have different DIN numbers assigned).

Table A1. Drug identification numbers for identification of OAT from PharmaNet

DIN/PIN	Description
999792, 66999990, 66999991, 66999992,66999993, 66999997, 66999998, 66999999, 67000000, 67000001,67000002, 67000003, 67000004, 67000005, 67000007, 67000008	DIN/PIN for methadone
2295695, 2295709, 2408090, 2408104, 2424851, 2424878, 2453908, 2453916, 2468085, 2468093	DIN/PIN for buprenorphine/naloxone
2242963, 2242964, 66999995, 66999996	DIN/PIN for buprenorphine
22123349, 22123346, 22123347, 22123348	DIN/PIN for SROM
66123367, 2146126, 22123340, 22123357	DIN/PIN for injectable OAT[†]

Abbreviations: DIN: Drug Identification Numbers; PIN: Product Identification Numbers; SROM: slow-release oral morphine; OAT: opioid agonist treatment; [†] Diacetylmorphine or hydromorphone dispensed in certain pharmacies.

Section A2: Data cleaning and processing

A2.1. Mortality data cleaning procedures

The Vital Statistics database is an administrative database that collects demographic and medical information on deaths. The cause of death variable is classified according to ICD10. Despite compulsory registration of all deaths in British Columbia, we found some discrepancy in deaths between records in Vital statistics database and hospital discharge from the Discharge Abstract Database or emergency department visits from the National Ambulatory Care Reporting System among those died in hospital. In addition, we found some medical administrative records in the Medical Service Plan, PharmaNet, the Discharge Abstract Database, and National Ambulatory Care Reporting System databases after the death date in Vital statistics. We identified and corrected these errors based on the proportion of medical records after death and gap time between the death date and the last medical service date. There were 7049 records of death from Vital Statistics, hospitalization discharge or emergency department visit data among 55 347 people who received OAT. Among those records, 19 deaths were classified as errors, leaving 7030 death records in the cohort (**Table A2**).

Table A2. Correction in the number of deaths in databases

	Deaths in VS and DAD/NACRS	Deaths in VS, not in DAD/NACRS	Deaths in DAD/NACRS, not in VS	Total deaths	Correction
Total	*x*	4513	*x*	7049	
Newborn deaths assigned to mother or deaths followed by health records*	*x*	0	*x*	19	Classified as error
Remaining deaths	2483	4513	33	7030	Confirmed death

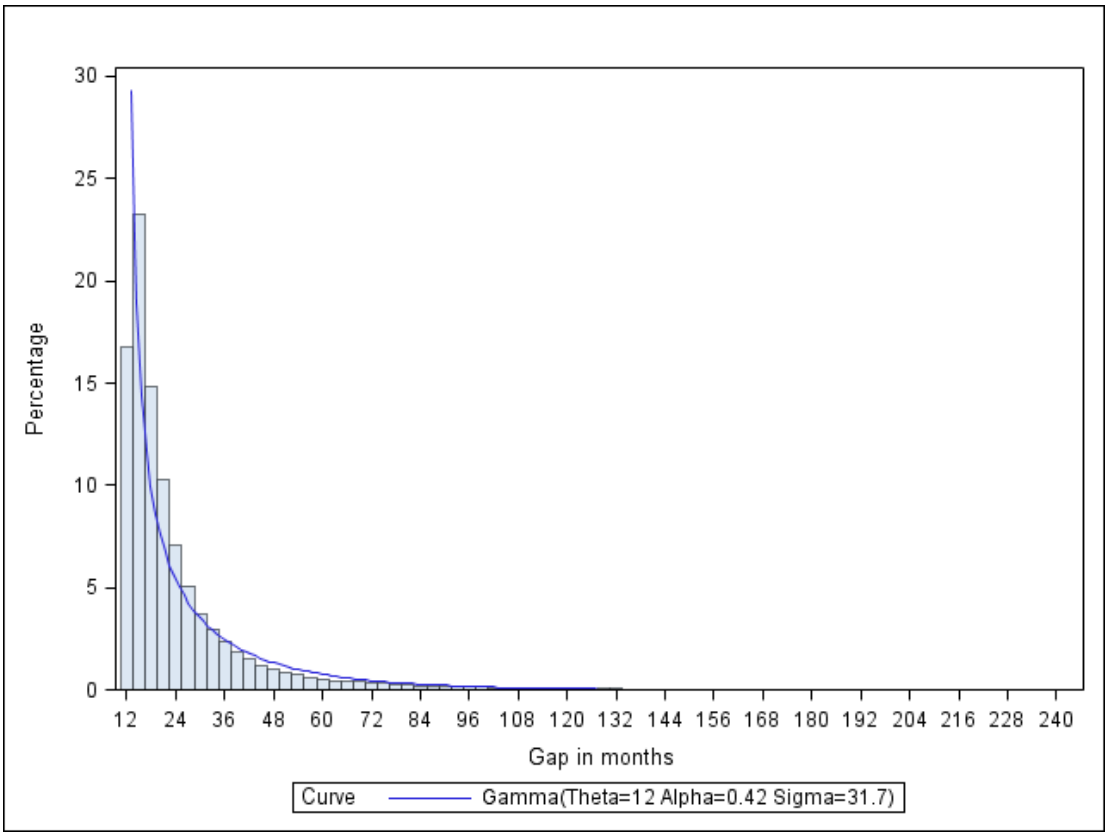
Abbreviations: VS: Vital statistics; DAD: Discharge Abstract Database (records of hospitalizations); NACRS: National Ambulatory Care Reporting System (records of emergency visits); *x*: suppressed due to small cell sizes <10, following the data sharing agreement. *More than 50% of records in each of MSP/NACRS/PharmaNet/DAD occurred after date of death and the last service date ≥ 90 days after death.

A2.2 Classifying administrative loss to follow-up

A limitation of research using BC's provincial health administrative data is that out-of-province migration is not captured explicitly. Without explicit consideration of loss to follow-up, the current number of people identified as having opioid use disorder and the number of person-years of follow-up may be inflated. Individuals lost to follow-up were defined as those without health service utilization recoded in the Discharge Abstract Database (hospitalization), Medical Service Plan (physician visits), or PharmaNet (drug dispensations) in the past 66 months (i.e. no record from April 1, 2013). The 66 month cut-off was determined empirically based on the distribution of gaps between episodes of health service utilization from hospitalization, Medical Service Plan, or PharmaNet claims. Specifically, we set the cut-off as the 75th percentile + 3 × interquartile range [75th percentile – 25th percentile][18] of the gaps greater than one year (**Figure A1**). We confirmed the cut-off by fitting a gamma distribution and identified a one-sided 95% confidence interval at 66 months.

We hypothesized that the majority of individuals who have been lost to follow-up have moved out of the province of BC. It is unlikely that they had died or otherwise engaged in the medical system, given our comprehensive data linkage with vital statistics and health administrative datasets.

Figure A1. Histogram of gaps (> 1 year) between health service utilization, with superimposed fitted gamma distribution curve



A2.3 PharmaNet database preparation

A2.3.1 OAT data cleaning procedures

OAT dispensation records were extracted from the PharmaNet database using the Drug Identification Number (DIN) or Product Identification Number (PIN; **Table A1**). Despite the high level of control in procuring and maintaining OAT records in PharmaNet, errors may arise. We sought to identify and, where possible, correct these errors, to produce most consistent and accurate OAT dispensation records possible. We created additional variables to facilitate the process of cleaning the dataset (**Table A3**). We captured a total of 41 704 201 OAT dispensations, and eight distinct types of human error were identified, pertaining to the days carried and quantity supplied fields. Comprehensive descriptions of the errors, along with resolutions were stated in **Table A4**. From 996 470 (2.4%) erroneous records, we corrected 689 814 (1.7%) of them, with 306 656 (0.7%) erroneous records remaining.

Table A3. PharmaNet variables and constructed variables used for cleaning OAT data

Variable	Description
PharmaNet variables	
dt_t	Date of service (i.e. Date of dispensation)
$days_t$	Days supply
qty_t	Quantity (mg/ml)
Constructed variables	
dt_{t-2}	Date of service (t-2)
dt_{t-1}	Date of service (t-1)
dt_{t+1}	Date of service (t+1)
dt_{t+2}	Date of service (t+2)
$days_{t-2}$	Days supply (t-2)
$days_{t-1}$	Days supply (t-1)
$days_{t+1}$	Days supply (t+1)
$days_{t+2}$	Days supply (t+2)
qty_{t-2}	Quantity (t-2)
qty_{t-1}	Quantity (t-1)
qty_{t+1}	Quantity (t+1)
qty_{t+2}	Quantity (t+2)
newdt	Corrected date of service
newdays	Corrected days supply
newqty	Corrected quantity

Table A4. Erroneous OAT dispensation records and resolutions

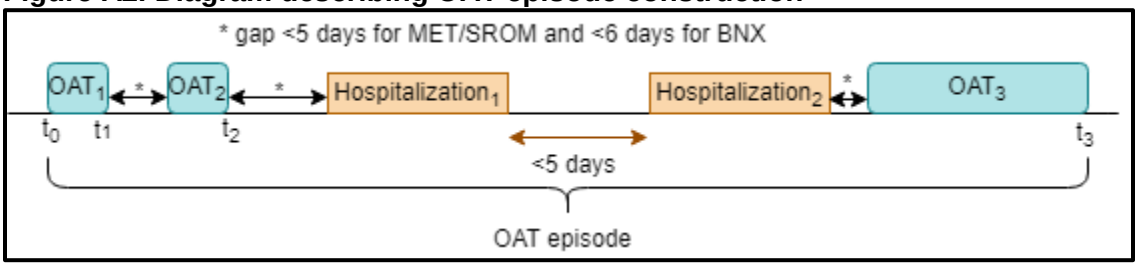
Error Type		Correction	Resolution	N corrected	Total corrected	% corrected
1. $days_t = 0$						
	10	$days_{t-1} = dt_t - dt_{t-1}$	newdays = $(qty_t/(qty_{t-1}/days_{t-1}))$	3	5	0.00%
	11	$0 < days_{t-1} < dt_t - dt_{t-1}$ $(qty_t/(qty_{t-1}/days_{t-1})) \leq (dt_{t+1} - dt_t)$		0		
	12	$days_{t+1} = dt_{t+2} - dt_{t+1}$	newdays = $(qty_t/(qty_{t+1}/days_{t+1}))$	2		
	13	$0 < days_{t+1} < dt_{t+2} - dt_{t+1}$ $(qty_t/(qty_{t+1}/days_{t+1})) \leq (dt_{t+1} - dt_t)$		0		
	14	$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t+1}/(dt_{t+2} - dt_{t+1}))$	newdays = $(dt_{t+1} - dt_t)$	0		
	15	$(dt_{t+1} - dt_t) \leq 30$ $(qty_t/(dt_{t+1} - dt_t)) \geq 0.5$		0		
2. $days_t \neq (dt_{t+1} - dt_t)$						
$(qty_{t-1}/days_{t-1}) \neq (qty_t/days_t)$	21	$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t-1}/days_{t-1})$	newdays = $(dt_{t+1} - dt_t)$	391 725	643 875	1.54%
	22	$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t-2}/days_{t-2}) = (qty_{t+1}/(dt_{t+2} - dt_{t+1}))$		3235		
		$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t-2}/days_{t-2}) = (qty_{t+1}/days_{t+1})$				
	23	$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t+1}/(dt_{t+2} - dt_{t+1})) = (qty_{t+2}/(dt_{t+3} - dt_{t+2}))$		40 084		
		$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t+1}/days_{t+1}) = (qty_{t+2}/days_{t+2})$				
		$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t+1}/(dt_{t+2} - dt_{t+1})) = (qty_{t+2}/days_{t+2})$				
		$(qty_t/(dt_{t+1} - dt_t)) = (qty_{t+1}/days_{t+1}) = (qty_{t+2}/(dt_{t+3} - dt_{t+2}))$				
	24	$(dt_{t+1} - dt_t) < days_t = qty_t$ or $(qty_{t-1}/days_{t-1}) \geq 5$		362		
	41	$(days_{t-1} + days_t) = dt_{t+1} - dt_{t-1}$	newdt = $(dt_{t-1} + days_{t-1})$	208 469		
3.						
$\lvert qty_t/days_t - qty_{t-1}/days_{t-1} \rvert > 10$ $\lvert qty_t/days_t - qty_{t+1}/(dt_{t+2} - dt_{t+1}) \rvert > 10$ $(dt_t - dt_{t-1}) \leq 30$ $(dt_{t+1} - dt_t) \leq 30$	31	$(qty_t/(qty_{t-1}/days_{t-1}))$ is an integer $(qty_{t-1}/days_{t-1}) = (qty_{t+1}/days_{t+1})$ $(qty_t/(qty_{t-1}/days_{t-1})) \leq 30$	newdays = $(qty_t/(qty_{t-1}/days_{t-1}))$	31 343	42 636	0.10%
		$(qty_t/(qty_{t-1}/days_{t-1}))$ is an integer $(qty_{t-1}/days_{t-1}) = (qty_{t+1}/(dt_{t+2} - dt_{t+1}))$				

	32	$qty_{t-1} = qty_t$ $(qty_{t-1}/days_{t-1}) = (qty_{t-2}/days_{t-2})$		4509		
	33	$qty_t/(qty_{t-1}/days_{t-1})$ is an integer $(qty_{t-1}/days_{t-1}) = (qty_{t-2}/days_{t-2})$ $(qty_t/(qty_{t-1}/days_{t-1})) \leq 30$		4545		
	38	$qty_t = qty_{t+1}$ $(qty_{t+1}/(dt_{t+2} - dt_{t+1})) = (qty_{t+2}/(dt_{t+3} - dt_{t+2}))$	newdays = $qty_t/(qty_{t+1}/(dt_{t+2} - dt_{t+1}))$	1132		
		$qty_t = qty_{t+1}$ $(qty_{t+1}/(dt_{t+2} - dt_{t+1})) = (qty_{t+2}/days_{t+2})$				
	39	$(qty_{t+1}/(qty_{t+1}/days_{t+1}))$ is an integer $(qty_{t+1}/(dt_{t+2} - dt_{t+1})) = (qty_{t+2}/(dt_{t+3} - dt_{t+2}))$		1107		
		$(qty_{t+1}/(qty_{t+1}/days_{t+1}))$ is an integer $(qty_{t+1}/(dt_{t+2} - dt_{t+1})) = (qty_{t+2}/days_{t+2})$				
4. $days_t > dt_{t+1} - dt_t$	51	$\lvert(qty_t/days_t) - (qty_{t-1}/days_{t-1})\rvert > 10$ $\lvert(qty_t/days_t) - (qty_{t+1}/(dt_{t+2} - dt_{t+1}))\rvert > 10$ $\lvert(qty_t/(dt_{t+1} - dt_t)) - (qty_{t-1}/days_{t-1})\rvert \leq 10$ $\lvert(qty_t/(dt_{t+1} - dt_t)) - (qty_{t+1}/(dt_{t+2} - dt_{t+1}))\rvert \leq 10$	newdays = $(dt_{t+1} - dt_t)$	3298	3298	0.01%
After correction			**Resolution**	**N remained**	**Total remained**	**% remained**
5. $days_t = 0$	60		[none]	0	0	0.00%
6. $days_t > dt_{t+1} - dt_t$	61		[none]	291 671	291 671	0.70%
7. $\lvert(qty_t/days_t) - (qty_{t-1}/days_{t-1})\rvert > 50$ $dt_t - dt_{t-1} \leq 30$	62	$qty_{t-1}/days_{t-1} = qty_{t+1}/days_{t+1}$	[none]	6573	11 336	0.03%
	63	$\lvert(qty_t/days_t) - (qty_{t+1}/days_{t+1})\rvert > 50$ and $[(qty_{t-2}/days_{t-2}) = (qty_{t-1}/days_{t-1})$ OR $(qty_{t+2}/days_{t+2}) = (qty_{t+1}/days_{t+1})]$	[none]	4763		
8. $(qty_t/days_t) > 500$ for methadone/	64		[none]	3649	3649	0.01%

A2.3.2 OAT episode construction

OAT episodes were constructed using the 'service date' and 'days supplied' fields in the PharmaNet database. Treatment episode length was calculated as the difference between the last and first days of dispensed medication within a period of continuous retention in treatment. Continuous OAT episodes had no interruptions in prescribed doses lasting ≥ 5 days for methadone or SROM, ≥ 6 days for buprenorphine/naloxone, and ≥ 3 days for injectable OAT, defined according to clinical guidelines for reversion to initiation dosing. Individuals might change their medication type during the continuing episode. We also adjusted for hospitalization in OAT episode construction, assuming that those who started OAT continued the treatment while in hospital (**Figure A2**). A total of 24 183 (7.8%) OAT episodes included a hospitalization, and among those episodes, median duration of hospitalization was 8 (interquartile range: 3 to 23) days.

Figure A2. Diagram describing OAT episode construction



OAT dispensations and hospitalizations with gaps less than the OAT discontinuation threshold were combined into one OAT episode. The duration of the OAT episode depicted in the figure is {t3 - t0}.

Section A3: Statistical analyses on mortality

A list of ICD-9 and ICD-10 codes used to determine underlying cause of death is provided in **Table A5.** ICD-9/ICD-10 codes used to identify concurrent chronic conditions are in **Table A6**. **Tables A7-A8** provides underlying data for mortality rates shown in **Figures 1-3** of the manuscript. **Table A9** shows the result of sensitivity analyses on the definition of death during OAT: (1) strictly by the date of OAT dispensation without incorporating hospitalization; and (2) treating deaths that occurred during the defined gap time for each medication as occurring during treatment.

Table A5. ICD-CA-9 and ICD-CA-10 codes used to identify concurrent chronic conditions*

Diseases	Diagnostic code	References
Mental health†	ICD-9 from DAD and MSP: 295-298, 300, 301, 308, 309, 311, 314; ICD-10 from DAD and NACRS: F20-F25, F28-F34, F38-F43, F48.8, F48.9, F60-F61, F69, F90; MSP additional diagnostic code 50B	(1), (2), (3), (4), (5), (6)
HIV	ICD-9 from DAD and MSP: 042-044, 079.53, 795.8, V08; ICD-10 from DAD and NACRS: B20-B24, B97.35, F02.4, O98.7, Z21; MSP fee item: 13015, 13105, 33645, 36370	(7), (8)
Hepatitis C virus	ICD-9 from DAD and MSP: 70.41, 70.51, 70.44, 70.54, 70.7; ICD-10 from DAD and NACRS: B17.1, B18.2, B19.2; AHFS category: 8:18.40	(9),(10),(11), (12)
Alcohol use disorder	ICD-9 from DAD and MSP: 291, 303, 305.0, 357.5, 425.5, 535.3, 571.0-571.3, 655.4, 760.71,V65.42; ICD-10 from DAD and NACRS: F10, Z50.2, Z71.4, Z72.1,G31.2, G62.1, G72.1, I42.6, K29.2, K70, K86.0, O35.4, P04.3, Q86.0; DIN: 2293269, 2158655, 2213826, 2444275, 2451883, 2534, 2542, 2041375, 2041391, 66124089, 66124085, 66124087	(13), (14)
Substance use disorder‡	ICD-9 from DAD and MSP: 292, 304.x (1-6,8,9), 305.x (2-4,6-9), 969.x (4,6,7), 970.81, E853.2, E854.1,E854.2, 648.3, 760.73, 760.75, 779.5; ICD-10 from DAD and NACRS: F12-F16, F19, X42, X62, Y12, T40.5, T40.7-T40.9, T42.4, T43.6, Z50.3, Z71.5, Z72.2, P04.4, P96.1	(1), (13), (15),(16)
Chronic pain§	ICD-9 from DAD and MSP: 338.2, 338.4, 307.80, 307.89, 338.0, 719.41, 719.45-719.47, 719.49, 720.0, 720.2, 720.9, 721.0-721.4, 721.6, 721.8, 721.9, 722, 723.0, 723.1, 723.3-723.9, 724.0-724.6, 724.70, 724.79, 724.8, 724.9, 729.0-729.2, 729.4, 729.5, 350, 352-357, 344.0, 344.1, 997.0, 733.0, 733.7, 733.9, 781; ICD-10 from DAD and NACRS: F45.4, G89.0, G89.2, G89.4, M08.1, M25.50, M25.51, M25.55-M25.57, M43.2-M43.6, M45, M46.1, M46.3, M46.4, M46.9, M47, M48.0, M48.1, M48.8, M48.9, M50.8, M50.9, M51, M53.1-M53.3, M53.8, M53.9, M54, M60.8, M60.9, M63.3, M79.0-M79.2, M79.6, M79.7, M96.1, G50, G52-G64, G82, G97, M89, R29	(2), (17), (18)

Abbreviations: ICD: International Classification of Diseases; DAD: Discharge Abstract Database (records of hospitalizations); NACRS: National Ambulatory Care Reporting System (records of emergency visits); MSP: Medical Service Plan (physician billing records); AHFS: American Hospital Formulary Service from PharmaNet; DIN: drug identification number. *To minimize misclassification due to errors in the coding of physician billing records, we applied a case finding algorithm based on the presence of at least 1 hospitalization, more than 3 physician billing records, or medication receipt for alcohol use disorder; †Any indication of depression, anxiety, psychotic illness, personality disorders, attention-deficit/hyperactivity disorders, or bipolar disorders; ‡Any indication of non-opioid drug use, poisoning (accidental or intentional), or substance use counselling or rehab, excluding alcohol use disorder; §non-cancer chronic pain.

Table A6. ICD-CA-9 and ICD-CA-10 codes used to determine underlying cause of death

Underlying cause of death	ICD-10 in Vital Statistics	ICD-10 in DAD/NACRS†	ICD-9 in DAD†	Description
Opioid-related	U: F11 or (U: X40-X44) & (I: T40.0-T40.4, T40.6)	M: F11 or (M: T40.0-T40.4, T40.6) & (E: X40-X44)	M: 304.0, 304.7, 305.5, or (M: 965.0) & (E: E850-E858)	**Opioid abuse or accidental opioid poisoning**
Drug-related	U: F11-F16, F19, X40-X44	M: F11-F16, F19, (M: T40, T42.4, T43.6) & (E: X40-X44)	M: 292,304,305.2-305.9, (M: 965.0, 969.4,969.5,970.81) & (E: E850-E858)	Drug abuse or accidental drug poisoning
Other external cause	U: V01-Y98 (except X40-X44)	M: S00-T98 except drug-related	M: 800-999 except drug-related	Injury, poisoning, and other consequences of external causes
Infectious disease	U: A00-B99	M: A00-B99	M: 001-139	Infectious and parasitic diseases
Other non-external cause	U: Any other codes	Any other codes	Any other codes	Any other non-external cause of death (e.g. chronic disease)
Unknown cause	U: R99	-	-	Unknown or inconclusive (cause of death still under investigation)

Abbreviations: ICD: International Classification of Diseases; DAD: Discharge Abstract Database; NACRS: National Ambulatory Care Reporting System; U: underlying cause of death; I: nature of injury code (ICD-10 codes starting with S or T); M: most responsible diagnosis; E: external cause in DAD. †ICD codes from DAD or NACRS were used if underlying cause of death from Vital Statistics was not available and the individual died in hospital.

Reference: Russolillo A, Moniruzzaman A, Somers JM (2018). Methadone maintenance treatment and mortality in people with criminal convictions: A population-based retrospective cohort study from Canada. PLoS Med 15(7): e1002625. https://doi. org/10.1371/journal.pmed.1002625

Table A7. Data underlying Figure 1

			All-cause			Drug-related*		Opioid-specific**	
		Person-years of follow-up	No. deaths	CMR† (95% CI)	SMR (95% CI)	No. deaths	CMR† (95% CI)	No. deaths	CMR† (95% CI)
On OAT, *overall*		202 315	2197	10.9 (10.4 to 11.3)	4.6 (4.4 to 4.8)	429	2.1 (1.9 to 2.3)	243	1.2 (1.1 to 1.4)
On OAT, *weeks since starting OAT*									
1	All	5414	77	14.2 (11.2 to 17.8)	7.7 (6.1 to 9.7)	34	6.3 (4.3 to 8.8)	23	4.2 (2.7 to 6.4)
	buprenorphine/naloxone	x	x	8.7 (3.8 to 17.2)	4.5 (1.9 to 8.8)	3	3.3 (0.7 to 9.5)	x	1.1 (0.0 to 6.1)
	methadone	4443	68	15.3 (11.9 to 19.4)	8.5 (6.6 to 10.8)	31	7.0 (4.7 to 9.9)	22	5.0 (3.1 to 7.5)
2	All	4452	73	16.4 (12.9 to 20.6)	8.7 (6.8 to 10.9)	15	3.4 (1.9 to 5.6)	10	2.2 (1.1 to 4.1)
	buprenorphine/naloxone	x	x	7.0 (2.3 to 16.4)	3.5 (1.1 to 8.2)	3	4.2 (0.9 to 12.3)	x	2.8 (0.3 to 10.2)
	methadone	3700	67	18.1 (14.0 to 23.0)	9.8 (7.6 to 12.5)	12	3.2 (1.7 to 5.7)	8	2.2 (0.9 to 4.3)
3-4	All	7437	75	10.1 (7.9 to 12.6)	5.3 (4.2 to 6.7)	17	2.3 (1.3 to 3.7)	11	1.5 (0.7 to 2.6)
	buprenorphine/naloxone	x	x	8.0 (3.7 to 15.2)	3.9 (1.8 to 7.4)	3	2.7 (0.5 to 7.8)	x	1.8 (0.2 to 6.4)
	methadone	x	66	10.6 (8.2 to 13.4)	5.7 (4.4 to 7.2)	14	2.2 (1.2 to 3.8)	x	1.4 (0.7 to 2.7)
5-12	All	21 120	228	10.8 (9.4 to 12.3)	5.6 (4.9 to 6.4)	34	1.6 (1.1 to 2.2)	21	1.0 (0.6 to 1.5)
	buprenorphine/naloxone	x	20	7.3 (4.4 to 11.2)	3.4 (2.1 to 5.3)	5	1.8 (0.6 to 4.2)	x	1.5 (0.4 to 3.7)
	methadone	18 207	202	11.1 (9.6 to 12.7)	5.9 (5.2 to 6.8)	27	1.5 (1.0 to 2.2)	16	0.9 (0.5 to 1.4)
>12	All	163 893	1744	10.6 (10.1 to 11.2)	4.3 (4.1 to 4.5)	329	2.0 (1.8 to 2.2)	178	1.1 (0.9 to 1.3)
	buprenorphine/naloxone	x	45	5.9 (4.3 to 7.8)	2.5 (1.8 to 3.3)	12	1.6 (0.8 to 2.7)	x	1.0 (0.4 to 2.1)
	methadone	155 516	1682	10.8 (10.3 to 11.3)	4.4 (4.2 to 4.6)	314	2.0 (1.8 to 2.3)	169	1.1 (0.9 to 1.3)
Off OAT, *overall*		198 502	4833	24.3 (23.7 to 25.0)	9.7 (9.5 to 10.0)	1755	8.8 (8.4 to 9.3)	1157	5.8 (5.5 to 6.2)
Off OAT, *weeks since stopping OAT*									
1	All	5263	712	135.3 (125.5 to 145.6)	73.9 (68.6 to 79.6)	260	49.4 (43.6 to 55.8)	168	31.9 (27.3 to 37.1)
	buprenorphine/naloxone	944	56	59.3 (44.8 to 77.0)	31.0 (23.4 to 40.2)	22	23.3 (14.6 to 35.3)	16	16.9 (9.7 to 27.5)
	methadone	4268	648	151.8 (140.4 to 164.0)	84.4 (78.0 to 91.2)	236	55.3 (48.5 to 62.8)	150	35.1 (29.7 to 41.2)
2	All	3419	130	38.0 (31.8 to 45.2)	20.6 (17.2 to 24.4)	32	9.4 (6.4 to 13.2)	22	6.4 (4.0 to 9.7)
	buprenorphine/naloxone	728	26	35.7 (23.3 to 52.4)	18.8 (12.3 to 27.5)	14	19.2 (10.5 to 32.3)	11	15.1 (7.5 to 27.1)
	methadone	2656	104	39.2 (32.0 to 47.4)	21.5 (17.6 to 26.0)	18	6.8 (4.0 to 10.7)	11	4.1 (2.1 to 7.4)
3-4	All	5025	185	36.8 (31.7 to 42.5)	19.8 (17.1 to 22.9)	52	10.3 (7.7 to 13.6)	39	7.8 (5.5 to 10.6)
	buprenorphine/naloxone	x	27	24.1 (15.9 to 35.1)	12.8 (8.4 to 18.6)	12	10.7 (5.5 to 18.7)	x	8.0 (3.7 to 15.3)

	methadone	3858	156	40.4 (34.3 to 47.3)	22.1 (18.8 to 25.9)	40	10.4 (7.4 to 14.1)	30	7.8 (5.2 to 11.1)
5-12	All	14 386	501	34.8 (31.8 to 38.0)	18.5 (16.9 to 20.2)	187	13.0 (11.2 to 15.0)	128	8.9 (7.4 to 10.6)
	buprenorphine/naloxone	3100	106	34.2 (28.0 to 41.4)	17.8 (14.6 to 21.6)	59	19.0 (14.5 to 24.5)	49	15.8 (11.7 to 20.9)
	methadone	11 180	387	34.6 (31.3 to 38.2)	18.6 (16.8 to 20.5)	128	11.4 (9.6 to 13.6)	79	7.1 (5.6 to 8.8)
>12	All	170 409	3305	19.4 (18.7 to 20.1)	7.5 (7.2 to 7.7)	1224	7.2 (6.8 to 7.6)	800	4.7 (4.4 to 5.0)
	buprenorphine/naloxone	17 822	355	19.9 (17.9 to 22.1)	9.0 (8.1 to 10.0)	162	9.1 (7.7 to 10.6)	123	6.9 (5.7 to 8.2)
	methadone	152 469	2942	19.3 (18.6 to 20.0)	7.3 (7.0 to 7.6)	1060	7.0 (6.5 to 7.4)	675	4.4 (4.1 to 4.8)

Abbreviations: CMR: crude mortality rate; SMR: standardized mortality ratio; CI: confidence interval; OAT: opioid agonist treatment; *x*: suppressed due to small cell sizes <10; *Death related to drug abuse or accidental drug poisoning; **Death related to opioid abuse or accidental opioid poisoning; †per 1000 person-years

Table A8. Data underlying Figure 2

	Person-years of follow-up	No. deaths*	CMR† (95% CI)	No. expected deaths	SMR (95% CI)
On OAT					
2010	10 073	88	8.7 (7.0,10.8)	21.6	4.1 (3.3,5.0)
2011	11 166	121	10.8 (9.0,12.9)	23.9	5.1 (4.2,6.1)
2012	12 153	102	8.4 (6.8,10.2)	26.4	3.9 (3.2,4.7)
2013	12 854	107	8.3 (6.8,10.1)	29.1	3.7 (3.0,4.4)
2014	13 345	125	9.4 (7.8,11.2)	31.7	3.9 (3.3,4.7)
2015	14 293	118	8.3 (6.8,9.9)	35.0	3.4 (2.8,4.0)
2016	15 677	129	8.2 (6.9,9.8)	42.2	3.1 (2.6,3.6)
2017	17 883	185	10.3 (8.9,11.9)	52.5	3.5 (3.0,4.1)
2018	14 456	164	11.3 (9.7,13.2)	43.5	3.8 (3.2,4.4)
Off OAT					
2010	9 143	179	19.6 (16.8,22.7)	21.6	8.3 (7.1,9.6)
2011	10 193	183	18.0 (15.4,20.8)	24.2	7.6 (6.5,8.7)
2012	11 568	221	19.1 (16.7,21.8)	27.8	8.0 (6.9,9.1)
2013	13 084	296	22.6 (20.1,25.4)	31.7	9.3 (8.3,10.5)
2014	14 927	258	17.3 (15.2,19.5)	36.8	7.0 (6.2,7.9)
2015	16 681	350	21.0 (18.8,23.3)	42.6	8.2 (7.4,9.1)
2016	18 505	564	30.5 (28.0,33.1)	51.6	10.9 (10.0,11.9)
2017	20 862	678	32.5 (30.1,35.0)	62.6	10.8 (10.0,11.7)
2018	17 578	532	30.3 (27.7,32.9)	51.7	10.3 (9.4,11.2)

Abbreviations: OAT: opioid agonist treatment; CMR: crude mortality rate per 1000 person-years; SMR: standardized mortality ratio; CI: confidence interval; *Actual number of observed deaths. Deaths with missing information on age and/or sex were excluded in SMR calculations; †Per 1000 person-years

Table A9. Relative risk of all-cause mortality among individuals accessing OAT, according to key periods of the opioid overdose public health emergency, by alternate OAT episode definitions: British Columbia, 01/01/1996-30/09/2018

	SA 1: OAT episode by dispensations only*	SA 2: Deaths during gap time defined as 'on OAT''
	Overall CMR (95% CI)	Overall CMR (95% CI)
On OAT	5.5 (5.2 to 5.8)	13.7 (13.2 to 14.2)
Off OAT	29.7 (28.9 to 30.4)	20.2 (19.6 to 20.8)
	Overall RR (95% CI)[†]	Overall RR (95% CI)[†]
	6.2 (4.9 to 7.7)	1.6 (1.4 to 1.7)
	RR (95% CI)[†]	RR (95% CI)[†]
Period 1: Prior to first fentanyl death[‡]	5.3 (4.4 to 6.4)	1.4 (1.3 to 1.5)
Period 2: First fentanyl death[§]	7.3 (5.6 to 9.7)	1.7 (1.5 to 2.0)
Period 3: PHE declaration[‖]	7.9 (5.8 to 10.8)	2.0 (1.7 to 2.4)

Abbreviations: SA: sensitivity analysis; OAT: opioid agonist treatment; CMR: crude mortality rate; CI: confidence interval; RR: rate ratio; PHE: public health emergency; *Deaths in hospital assigned as 'off OAT'; [†]Risk ratio comparing crude all-cause mortality rate by OAT status (off OAT versus on OAT), adjusting for age, sex, medication type (buprenorphine/naloxone only, methadone only), OAT period (≤4 weeks or >4 weeks since starting or stopping OAT). [‡]Beginning of follow-up (01/01/1996) to the day prior to the first fentanyl death in British Columbia (31/03/2012); [§]Date of the first fentanyl death in British Columbia (01/04/2012) to the day before the PHE declaration (13/04/2016); [‖]Date of the PHE declaration (14/04/2016) to the end of follow-up (30/09/2018).

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